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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,107	10/30/2001	Grant L. Schoenhard	13726US01	8970

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/000,107	SCHOENHARD, GRANT L.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-47 and 56-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group VIII in the reply filed on March 5, 2004 is acknowledged. Applicant stated that the election was made with traverse, however applicant failed to state a grounds for the traversal. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-47 and 56-62 are withdrawn from consideration. Claims 48-55 are under consideration in this office action.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

4. The disclosure is objected to because of the following informalities: The attempt to incorporate subject matter into this application by reference to the many commercial databases such as http:/www.mdli.com at page 42 is improper because Applicants have embedded a hyperlink which is impermissible and requires deletion. This attempt to incorporate subject matter into the patent by reference is improper because PTO policy does not permit the PTO to link to any commercial sites since the PTO exercises no control over those organizations, views or accuracy of the information contained on those outside sites. Appropriate correction is required

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 48-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In particular, claim 48 is directed to a composition for the treatment of a microbial infection comprising: a) an opioid inhibitor of an ABC drug transporter; and b) an anti-microbial agent wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein.

The instant specification fails to provide any experiments that show that such a composition comprising: a) an opioid inhibitor of an ABC drug transporter; and b) an anti-microbial agent wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein would be effective for treating any microbial infection in a human or any other animal. There is no teaching of the claimed composition. There is no teaching of ratios that teach how much opioid inhibitor of an ABC drug transporter and how much anti-microbial agent should be in the claimed

composition. Moreover, the term "treatment of a microbial infection" encompasses the ability of the composition to induce treatment against any bacterial, viral, fungal, parasitic, yeast, any infection or any disease induction however there is no teaching the a composition would be capable of said treatment. The art of microbial infection is highly unpredictable and the instant specification fails to provide any information that the recited composition would provide any type of treatment to any type of patient against any type of microbial infection. There are no immunological experiments provided to demonstrate that the claimed composition is capable of mounting treatment against microbial infections response. More importantly, there are no challenge experiments to demonstrate that an animal was treated with the claimed composition and was then thereby protected from any microbial infection.

There are no protocols provided which demonstrate that the claimed composition would be effective in treatment, nor are the protocols detailing the amount of composition needed to treat against any microbial infection. There is no teaching as to what the most effective route of administration for the claimed composition would be. There are merely general outlines that do not apply directly to the instant invention. The specification at pages 10-11 only discloses predictive compositions. Examples 1-6 fail to teach a composition comprised of a) an opioid inhibitor of an ABC drug transporter; and b) an anti-microbial agent. At best, the specification teaches co-administration of an opioid inhibitor of an ABC drug transporter and an anti-microbial agent, however co-administration is not equivalent to a composition comprising an opioid inhibitor of an ABC drug transporter and an anti-microbial agent. The specification and claims fail to

recite: subjects for which the composition can be administered, dosage schemes, administration modes and the like. Therefore the specification fails to provide support for the claims. It is noted that it is well known that merely generating an immune response does not equate to treatment of microbial infections. Applicants' have not demonstrated that the claimed composition comprising an opioid inhibitor of an ABC drug transporter; and an anti-microbial agent will provide treat against each and every or even one type of microbial infection in a recipient.

This demonstration is required for the skilled artisan to be able to use the claimed composition for their intended purpose of treating microbial infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed composition, i.e. would not be able to accurately predict if treatment has been induced against a microbe. Furthermore, the specification fails to adequately disclose a description of the claimed composition, thus a skilled artisan would be required to de novo locate, identify and characterize the claimed composition with the recited abilities.

Accordingly, this would require undue experimentation given the fact that the specification is completely lacking in teachings as to claimed composition with the broadly claimed treatment characteristics. Thus, the art indicates that it would require undue experimentation to formulate and use a successful composition without the prior demonstration of efficacy.

6. Claims 48-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Acronyms like ABC must be spelled out when used for the first time in a chain of claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 48-52 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minoia et al., (US Patent 5,811,451). The claims are drawn to a composition for the treatment of a microbial infection comprising: a) an opioid inhibitor of an ABC drug transporter; and b) an anti-microbial agent wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein. The dependant claims are drawn to specific anti-microbial agents, chemical formulas for the drug, and specific opioid inhibitors.

Minoia et al., teach the combined use of opiate antagonist for the preparation of medicaments for the treatment of endorphrin-related pathologies (col. 1 lines 5-10). Opiate antagonist which were used include nalbuphine, betachloronaltrexonine, naltrexonazine, naloxone, nalmefene, beta-funaltrexamine, naloxazone, ICI 174.864, 7-benzylidenenaltrexone (BNTX), naltrindole, norbinaltorphammine, naltribene (NTB),

MR-2266, 5'-NTII and LY 27614 (col. 3 lines 53-65). It is noted that the instant specification and claims define opioid inhibitors of the ABC drug transporters are selected from the group consisting of naltrexone, naloxone and nalmefene. Thus, the opioid inhibitors cited by Minoia et al., have the claimed compound formula and meet the qualifications as homologues of PGP1a. The choice of opioids will depend on several factors such as kinetics, potency, safety, pharmological risk and the like (col. 3 lines 48-50). For instance, acute pathologies use the fast action short half life drugs such as naloxone, while chronic pathologies use long lasting drugs such as naltrexone (col. 3 lines 50-53). Example 5 teaches treating distemper in a dog with naloxone and antibiotics cephalosporins and aminoglycosides.

Therefore it is prima facie obvious to combine the opioid inhibitor of an ABC drug transporter; and an anti-microbial agent taught by Minoia et al., each of which is taught to be useful for the same purpose of treating an animal with a microbial infection, in order to form the claimed composition to be used for the very same purpose of treatment and the idea of combining them flows logically from their having been taught in the prior art as useable together. No more than routine skill would have been required to use the claimed opioid inhibitor of an ABC drug transporter; and an anti-microbial agent when they have been taught as useful together in an old process to achieve the expected and beneficial results found when using the separate compounds in a single composition. Moreover, there would have been a reasonable expectation of success since Minoia et al., already teach the combined use of opioid drugs for the treatment of several microbial pathologies.

8. Claims 48-52 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernstein (US Patent 4,466,968). The claims are drawn to a composition for the treatment of a microbial infection comprising: a) an opioid inhibitor of an ABC drug transporter; and b) an anti-microbial agent wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein. The dependant claims are drawn to specific anti-microbial agents, chemical formulas for the drug, specific opioid inhibitors.

Bernstein (US Patent 4,466,968) teaches a method for prophylaxis or treatment of emesis and nausea. Naloxone is a narcotic antagonist used in the treatment of itching, reduction of nausea and vomiting (col. 1 lines 20-35). Naloxone was administered before dicarbazine, adriamycin or methotrexate (col. 1 lines 37-42). Example IX teach naloxone administration for viral gastroenteritis. Example XIII teaches the administration of naltrexone followed by the administration of the anti-microbial erythromycin. Example XV teach the administration of naloxone followed by the anti-microbial tetracycline administration. It is noted that the instant specification and claims define opioid inhibitors of the ABC drug transporters can be naltrexone or naloxone. Thus, the opioid inhibitors cited by Bernstein have the claimed compound formula and meet the qualifications as homologues of PGP1a.

Therefore it is prima facie obvious to combine the opioid inhibitor of an ABC drug transporter; and an anti-microbial agent taught by Bernstein each of which is taught to be useful for the same purpose of treating an animal with a microbial infection, in order to form the claimed composition to be used for the very same purpose of treatment and

the idea of combining them flows logically from their having been taught in the prior art as useable together. No more than routine skill would have been required to use the claimed opioid inhibitor of an ABC drug transporter; and an anti-microbial agent when they have been taught as useful together in an old process to achieve the expected and beneficial results found when using the separate compounds in a single composition. Moreover, there would have been a reasonable expectation of success since Bernstein already teaches the combined use of opioid drugs for the treatment of microbial infections.

Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Gekker et al., teach naltrexone potentiates anti-HIV-1 activity of antiretroviral drugs.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 10, 2003

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